

# **SPL Process ER/DL Meeting Meeting Minutes Feb 25, 2015**

**Chair of today's meeting:** Herb O'Brien

Teleconference information:

USA Toll-Free 866-213-2145

USA Paid/International: 609-454-9913

Access code: 273 8216

Teleconference information: How to mute/unmute

#6: Mute

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Link to the SPL wiki:

<http://spl-work-group.wikispaces.com/share/view/51351516>

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## **1. Pregnancy Lactation and Labeling Rule (PLLR) Approved Dec 2014**

Summary of rule

- Pregnancy Categories eliminated and replaced by a risk summary
- Pregnancy and labor delivery subsections are merged into a single pregnancy subsection 8.1 of the label.
- If there is a scientifically acceptable pregnancy registry, this subsection must contain information about the registry, contact information to enroll or to obtain more information about the registry.
- The Pregnancy subsection is reorganized to include a summary risks of using the drug during pregnancy.
- The risk summary replaces the current letter categories
- Must include information on all adverse development outcomes from all relevant data sources
- Clinical Considerations section added to help healthcare providers make prescribing decisions and counsel women about use of the drug during pregnancy. Information on labor and delivery would be included here.
- Data section would include data supporting the risk summary
- Nursing Mothers section is renamed lactation (8.2) and provides known information about breast feeding.
- Females and Males of Reproductive Age (8.3) contains information about the need for pregnancy testing, contraception recommendations and infertility information as related to the drug,

- In addition the PLLR

**What it mean for us:**

- New headings and subsections with new Loinc Codes:

## **8.1 Pregnancy**

### ***Pregnancy Exposure Registry***

Omit this section if not applicable.

### ***Risk Summary***

### ***Clinical Considerations***

*Disease-associated maternal and/or embryo/fetal risk (omit if not applicable)*

*Dose adjustments during pregnancy and the postpartum period (omit if not applicable)*

*Maternal adverse reactions (omit if not applicable)*

*Fetal/Neonatal adverse reactions (omit if not applicable)*

*Labor or delivery (omit if not applicable)*

### ***Data***

*Human Data (omit if not applicable)*

*Animal Data (omit if not applicable)*

## **8.2 Lactation**

***Risk Summary (required subheading)***

***Clinical Considerations (omit if not applicable)***

***Data (omit if not applicable)***

## **8.3 Females and Males of Reproductive Potential**

(omit if none of the subheadings are applicable)

***Pregnancy Testing (omit if not applicable)***

***Contraception (omit if not applicable)***

***Infertility (omit if not applicable)***

- Goes into effect as of June 30 2015. Drugs submitted after this date will use the new format immediately. Previously approved drugs approved on or after June 30, 2001 will have a phased in implementation schedule from 3 to 5 years. Generics must be updated at the time of the reference drug. I will attach the implementation schedule to the meeting minutes.

Applications required to conform to new pregnancy/lactation content requirements	Time by which labeling with new pregnancy/lactation content must be submitted to FDA for approval
New or Pending Applications	
Applications submitted on or after the effective date of the pregnancy final rule	Time of submission.
Applications pending on the effective date of the pregnancy final rule	4 years after the effective date of pregnancy final rule or at time of approval, whichever is later.
Approved Applications Subject to the Physician Labeling Rule	
Applications approved any time from June 30, 2001, up to and including June 29, 2002, and from June 30, 2005, up to and including June 29, 2007	3 years after the effective date of pregnancy final rule.
Applications approved any time from June 30, 2007, up to and including the effective date of the pregnancy final rule	4 years after the effective date of pregnancy final rule.
Applications approved from June 30, 2002, up to and including June 29, 2005	5 years after the effective date of pregnancy final rule.

**2. Question from David Shilling on Bulk and API Drug Listings**

- FDA's database containing drug listed bulk finished good pharmaceuticals as well as API is not publically available, is there a mechanism in place to retrieve these listings?
- The data is available but currently must be requested through the FDA's Freedom of Information office: <http://www.fda.gov/RegulatoryInformation/FOI/default.htm>  
There plans in the future to include this data in the NDC Directory or publish this data in a similar fashion, but that will not occur anytime soon.
- Confirmation of drugs that are not in their final dosage form (ie. APIs and bulk drugs) can be obtained by emailing [EDRLS@FDA.gov](mailto:EDRLS@FDA.gov) with the drug name and NDC number.

**3. Establishment Registration Question from Ben Harpster:**

Part A: A site in the U.S. will only be manufacturing for the rest of the world, not the U.S. market. Does it need to have an establishment registration? If yes, what regulation says this?

FDA Compliance Officer Response: The site does not have to be registered under these circumstances

Part B: The above site is being provided API from outside the U.S. Can the API manufacturer be inspected by the FDA, even though it will not be used in the manufacture of U.S. marketed product? Which regulation says this?

**FDA Compliance Officer Response:** The API manufacturer can be inspected by FDA if they make the API under consideration in this case for another domestic firm producing the dosage form.

Also, the foreign API supplier could be making different APIs used for domestically produced dosage form products. This could result in inspection.

These are the only two circumstances which I can think of meriting inspection of the API firm.

My Comment to Ben: Please contact [EDRLS@fda.hhs.gov](mailto:EDRLS@fda.hhs.gov) directly with these questions. I have heard a variety of opinions regarding the questions and provide us with a follow-up.

### **Who Must Register**

The owner or operator of an establishment entering into the manufacture, preparation, propagation, compounding, or processing (which includes, among other things, repackaging and relabeling) of a drug or drugs<sup>14</sup> and not exempt under section 510(g) of the Act or subpart B of 21 CFR part 207, must register the establishment with FDA within 5 days after beginning the operation (21 CFR 207.21(a) and 21 CFR 207.3(a)(8)).

### **Sec. 207.40 Establishment registration and drug listing requirements for foreign establishments.**

(a) Foreign drug establishments whose drugs are imported or offered for import into the United States shall comply with the establishment registration and drug listing requirements in subpart C of this part, unless exempt under subpart B of this part or unless the drugs enter a foreign trade zone and are re-exported from that foreign trade zone without having entered U. S. commerce.

No drug may be imported into or offered for import into the United States unless it is listed as required in subpart c of this part and manufactured, prepared, propagated at a registered foreign drug establishment

### **IMPORT FOR EXPORT PROVISIONS FOR PRODUCTS MANUFACTURED IN FOREIGN TRADE ZONES**

Foreign Trade Zones are federally sanctioned sites that, only for tariff purposes, are considered outside of the "Customs territory" of the United States. Nevertheless, products stored or manufactured in a Foreign Trade Zone are within the territory of the United States for the purposes of the Act and are expected to meet the same requirements as other products regulated by FDA [see Compliance Policy Guides 110.600 "FDA Authority Over Products of Foreign Origin Located in Foreign Trade Zones, Bonded

Warehouses, or on Bonded Carriers", and 110.200 "Export of FDA Regulated Products from U.S. Foreign Trade Zones"). These include the requirements of section 801(d)(3) and section 801(d)(4).

This sounds like it might be an import for export – and might be covered by those requirements.

<http://www.fda.gov/ICECI/ComplianceManuals/RegulatoryProceduresManual/ucm179481.htm>

as well as section 801 of FD&C?

<http://www.fda.gov/RegulatoryInformation/Legislation/FederalFoodDrugandCosmeticActFDCAAct/FDCAActChapterVIIIImportsandExports/ucm107032.htm>

Meeting Discussion:

- There is a category “for Export Only”, for drug listing product for export only.
- Actually a final product...
- Used a file type of Human Prescription Drug without highlights – therefore needed to add a section of text – used temperature range.
- Suggestion – manufactured exclusively for private label distributor
- See NDC on Daily Med: 0173707700

Ben Harpster to follow-up and report back. Here is GSK product for export only on Daily Med

<http://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=3fdc827c-182f-435c-a576-ba90d452ec7e>

#### 4. D&B presentation and contact

Question from Donna Alvarez: Back in December we were told a rep from Dun & Bradstreet would participate on one of the calls to discuss how we can work with them, and what the process would be, to update the DUNS information in their database. Are there any plans to have a D&B rep participate in the near future?

I have a representative will to attend one of our meetings. Lonnie has recommended we contact Ryan Paul of D&B. His e-mail address is: [PaulR@DNB.com](mailto:PaulR@DNB.com).

**Discussion:** Several companies have been contacted to help test out a link to see if our spl will validated.

- Links work really well.

- Put in one site at a time on the input screen. Then hit validate.
- If it doesn't match, then will not tell you which part is wrong. But it will tell you if the DUNS number doesn't match. Very helpful.
- There is a German site that has a program that will validate DUNS numbers and company names/address. The site will give you feedback on what DnB has in the DUNS database.

D&B Qualifying System: <https://dunsvalidation.azurewebsites.net/login.aspx>

German D&B Site:

[https://www.upik.de/8a6fa073c9feb2d4f205e7913a50004a/en/upik\\_suche.cgi?searchAgaIn=1](https://www.upik.de/8a6fa073c9feb2d4f205e7913a50004a/en/upik_suche.cgi?searchAgaIn=1)

## 5. Marketing Start Dates

- Kathy Lins is now outsourcing SPL. They don't have a market launch date when they need to send out the documents for conversion. Has anyone used an approximate market launch date?
  - People use a variety of dates – approval date, or approximate market start date.
  - There is no problem either way.
  - Alternative: List it now with a far in the future date....then relist it close to launch with a real date (this accomplishes 2 things – you get it in, and make sure that the file passes validation). They don't go into the NDC directory or on Daily Med until the actual market start date.
  - If you use a date that is close...and it gets drug listed....then it will appear in the NDC directory and on Daily Med. The only way to get it off is to delist it – then you can't use the NDC code for another product for 5 years. Be careful here.
  - You can also use the approval date.

## 6. Lot Distribution SPL

- Are vendors ready to create the SPL?
- Vendors are getting ready. They need to know what is required. It looks like additional information is required. Would like to talk about this at the next team meeting. How would the conversion business get the information that they need to create the SPL – therefore the SPL needs to be in the data provided.
- See pdf page 130, 129 in the SPL implementation guide. – for a plain English description of what information is required. Some information is coming from the drug listing. But they need to be able to link the lot distribution data with the drug listing.